

PTO/SB/08a (05-03)

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 1 of 9

Complete if Known

Application Number	10/674,666
Filing Date	September 29, 2003
First Named Inventor	Mike Clark
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
C.E.	A	US-6,183,738	02/06/2001	Clark	
	B	US- 4,179,337	12/18/1979	Davis et al	
	C	US- 4,609,546	09/02/1986	Hiratani	
	D	US- 5,372,942	12/13/1994	McGarity et al	
	E	US- 5,447,722	09/05/1995	Lang et al	
	F	US- 5,468,478	11/21/1995	Saifer et al	
	G	US- 5,474,928	12/12/1995	Takaku et al	
	H	US- 5,804,183	08/08/1998	Filpula et al	
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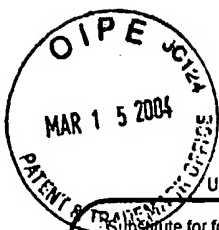
FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Y ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
C.E.	I	EP 0 372 752 A2	06/13/90	Genentech		
	J	JP 2-053490	02/90	Agen Ind. Sci. Tech.		X
	K	JP 4-121187	04/92	Nippon Mining		X
	L	WO94/05332	03/17/94	Berlex		
	M	WO96/34015	10/31/96	Boehringer Ingelheim		

Examiner Signature	C.E.	Date Considered	11/22/04
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PTO/SB/08b(05-03)

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 2 of 9

Complete if Known

Application Number	10/674,666
Filing Date	September 29, 2003
First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ele	A1	SUN, et al., "Incidence and cofactors of hepatitis C virus-related hepatocellular carcinoma: a prospective study of 12,008 men in Taiwan," Am. J. Epidemiol. (2002) 157:674-682.	
	A2	HERRINE, "Approach to the patient with chronic hepatitis C virus infection," Ann. Intern. Med. (2002) 136:747-757.	
	A3	HOOFNAGLE, "Course and outcome of hepatitis C," Hepatology (2002) 36:S21-S29.	
	A4	LAUER and WALKER, "Hepatitis C virus infection," (2001) N.Engl. J. Med. (2001) 345:41-52.	
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	A8	YOSHIZAWA, "Hepatocellular carcinoma associated with hepatitis C virus infection in Japan. Projection to other countries foreseeable future," Oncology (2002) 62 (Supp. 1):8-17.	
	A9	COLOMBO, "Natural history and pathogenesis of hepatitis C virus related hepatocellular carcinoma," J. Hepatol. (1999) 31 (Supp 1):25-30.	
	A10	EL-SERAG, "Hepatocellular carcinoma and hepatitis C in the United States," Hepatology (2002) 36:S74-S83.	
✓	A11	RYDER, "Guidelines for the diagnosis and treatment of hepatocellular carcinoma (HCC) in adults," Gut (2003) 52 (Supp III):iii1-iii8.	

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ele

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 3 of 9

Complete if Known

Application Number	10/674,666
Filing Date	September 29, 2003
First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

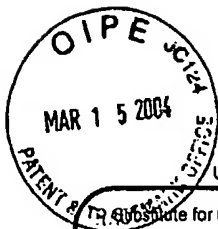
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ele	A12	EL-SERAG, "Global epidemiology of hepatocellular carcinoma," Clin. Liver Dis. (2001) 5:87-107.	
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	A19	SUGIMURA, et al., "High sensitivity of human melanoma cell lines to the growth inhibiting activity of Mycoplasma arginini deaminase in vitro," Melanoma Res. (1992) 2:191-198.	
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	A21	SNYDERMAN, et al., "The arginine requirement of the infant," J. Dis. Child (1959) 97:192.	
U	A22	SHEN, et al., "Resistance to the anti-proliferative activity of recombinant arginine deaminase in cell culture correlates with the endogenous enzyme, argininosuccinate synthetase," Cancer Lett. (2003) 191:165-170.	

Examiner Signature	ele	Date Considered	11/22/04
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Substitute for form 1449A/PTO		Complete if Known	
		Application Number	10/674,666
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Filing Date	September 29, 2003
		First Named Inventor	Mike Clark
		Group Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
		Attorney Docket Number	PHOE0001-100
Sheet	4	of	9

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ele	A23	FALCK-YTTER, et al., "Surprisingly small effect of antiviral treatment in patients with hepatitis C," Ann. Intern. Med. (2002) 136:288-292.	
	A24	FRIED, "Side effects of therapy of hepatitis C and their management," Hepatology (2002) 36:S237-S244.	
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	A29	CHANDLER, et al., "Treatment of chronic hepatitis C: a systematic review," Hepatology (2002) 36:S135-S144.	
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Examiner Signature	ele	Date Considered	11/22/04
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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 5 of 9

Complete if Known

Application Number	10/674,666
Filing Date	September 29, 2003
First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
el	A34	McHUTCHINSON, et al, "Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C," N. Eng. J. Med. (1998) 339:1485-1492.	
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	A38	CHRISTIE and CHAPMAN, "Combination therapy for chronic hepatitis C: interferon and ribavirin," Hosp. Med. (1999) 60:357.	
	A39	ROUSE, et al., "Dependence of adenovirus replication on arginine and inhibition of plaque formation by pleuropneumonia-like organisms," Virology (1963) 20:357-365	
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	A42	MINIMISHIMA and BENYESH-MELNICK, "Arginine-dependent events in cytomegalovirus infection," Bacteriol. Proc. (1969) 170:334-339.	
	A43	LEVINE, et al., "Late stage synchronization of respiratory syncytial virus replication," Virology (1971) 45:390-400.	
	A44	WINTERS, et al., "A non-functional arginine biosynthetic pathway in polyoma-infected mouse embryo cells," Biochem. Biophys. Res. Comm. (1972) 47:1045-1051.	

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Signature

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**INFORMATION DISCLOSURE
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Sheet 6 of 9

Compleat if Known

Application Number	10/674,666
Filing Date	September 29, 2003
First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

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ele	A45	IINUMA, et al., "Studies on the assembly of Newcastle disease virus: an arginine-dependent step in virus replication," Virology (1973) 51:205-215.	
	A46	ROMANO and SCARLATA, "Amino acid requirements of measles virus in HeLa cells," Arch. Gesamte Virus Forschung (1973) 43:359-366.	
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✓	A55	GILL, et al., "Inhibition of cell division in L5178Y cells by arginine-degrading mycoplasmas: the role of arginine deaminase," Can. J. Microbiol. (1970) 16:415-419.	

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Sheet 7 of 9

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First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

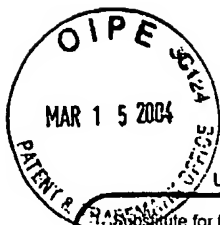
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ele	A56	HERSHFIELD, et al., "Treatment of adenosine deaminase deficiency with polyethylene glycol-modified adenosine deaminase," N. Eng. J. Med. (1987) 316:589-598.	
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	A63	MISAWA, et al., "High-level expression of Mycoplasma arginine deaminase in Escherichia coli and its efficient renaturation as an anti-tumor enzyme," J. Biotechnol. (1994) 38:145-155.	
	A64	MIYAZAKI, et al., "Potent growth inhibition of human tumor cells in culture by arginine deaminase purified from a culture of a Mycoplasma-infected cell line," Cancer Res. (1990) 50:4522-4527.	
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Examiner Signature	ele	Date Considered	11/22/04
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Complete if Known	
		Application Number	10/674,666
		Filing Date	September 29, 2003
		First Named Inventor	Mike Clark
		Group Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
Sheet 8 of 9	Attorney Docket Number	PHOE0001-100	

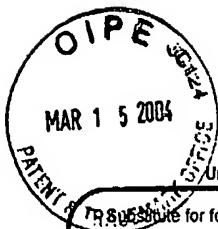
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ele	A67	OGINSKY, "Isolation and determination of arginine and citrulline," Meth. Enzymol. (1957) 3:639-642.	
	A68	OHNO, et al., "Cloning and nucleotide sequence of the gene encoding arginine deaminase of Mycoplasma arginini," Infect. Immun. (1990) 58:3788-3795.	
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	A71	SAYERS, et al., "Rapid high-efficiency site-directed mutagenesis by the phosphorothioate approach," Biotechniques (1992) 13:592-596.	
	A72	STOCKS, et al., "A fluorimetric assay of the degree of modification of protein primary amines with polyethylene glycol," Anal. Biochem. (1986) 154:232-234.	
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↓	A77	ZALIPSKY, et al., "Use of functionalized poly(ethylene glycol)s for modification of polypeptides," Polyethylene Glycol Chemistry: Biotechnical and Biomedical Applications, Harris, ed., Plenum, NY, 1992, pp. 347-370.	

Examiner Signature	ele	Date Considered	11/22/04
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STATEMENT BY APPLICANT**

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Sheet 9 of 9

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First Named Inventor	Mike Clark
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	PHOE0001-100

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ele	A78	DILLON, et al., "Biochemical characterization of the arginine degrading enzymes arginase and arginine deaminase and their effect on nitric oxide production," Med. Sci. Monit. (2002) 8:CR248-CR253.	
↓	A79	THOMAS, et al., "Enzymic degradation of plasma arginine using arginine deaminase inhibits nitric oxide production and protects mice from the lethal effects of tumour necrosis factor alpha and endotoxin," Biochem. J. (2002) 363:581-587.	

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